Appl. No. 10/699,562 Amdt. dated September 13, 2007 Amendment under 37 CFR 1.116 Expedited Procedure Examining Group 1618

Listing of the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1	1 (currently amended): A molecule of the structure $\mathbf{A} - \mathbf{X} - \mathbf{B}$, wherein
2	B is a peptide portion of about 5 to about 20 basic amino acid residues, which is
3	suitable for cellular uptake,
4	A is a peptide portion of about 2 to about 20 acidic amino acid residues, which
5	when linked with portion $\bf B$ is effective to inhibit or prevent cellular uptake of portion $\bf B$, and
6	X is a linker of about 2 to about 100 atoms joining A with B, which can be
7	cleaved under physiological conditions, wherein X comprises the sequence of SEQ ID NO: 1.
1	2 (original): The molecule of claim 1, wherein said peptide portion A comprises
2	about 5 to about 9 glutamates or aspartates.
1	3 (original): The molecule of claim 2, wherein said peptide portion A comprises
2	about 5 to about 9 consecutive glutamates or aspartates.
1	4 (original): The molecule of claim 1, wherein said peptide portion B comprises
2	about 9 to about 16 arginines.
1	5 (original): The molecule of claim 4, wherein said peptide portion B comprises
2	about 9 to about 16 consecutive arginines.
1	6 (original): The molecule of claim 1, wherein said peptide portion A comprises
2	D-amino acids.
1	7 (original): The molecule of claim 1, wherein said peptide portion B comprises
2	D-amino acids.

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1	8 (original): The molecule of claim 1, wherein said peptide portion A consists of
2	D-amino acids.
1	9 (original): The molecule of claim 1, wherein said peptide portion B consists of
2	D-amino acids.
1	10 (original): The molecule of claim 1, wherein said peptide portions A and B
2	consists of D-amino acids.
1	11 (currently amended): A molecule for transporting a cargo moiety across a cell
2	membrane of the structure $A - X - B - C$, wherein
3	C is a portion comprising a cargo moiety,
4	B is a peptide portion of about 5 to about 20 basic amino acid residues, which is
5	suitable for cellular uptake, is covalently linked to portion C, and is effective to enhance
6	transport of cargo portion C across a cell membrane,
7	A is a peptide portion of about 2 to about 20 acidic amino acid residues, which
8	when linked with portion ${\bf B}$ is effective to inhibit or prevent cellular uptake of ${\bf B}$ - ${\bf C}$, and
9	X is a cleavable linker of about 2 to about 100 atoms joining A with $\mathbf{B} - \mathbf{C}$, which
10	can be cleaved under physiological conditions, wherein X comprises the sequence of SEQ ID
11	NO: <u>1</u> .
1	12 (original): The molecule of claim 11, wherein said peptide portion A
2	comprises amino acids selected from the group of acidic amino acids consisting of glutamate and
3	aspartate.
1	13 (original): The molecule of claim 11, wherein said peptide portion B
2	comprises amino acids selected from the group of basic amino acids consisting of arginine and
3	histidine.
1	14 (original): The molecule of claim 11, wherein said cargo portion C is selected
2	from the group of cargo moieties consisting of a fluorescent moiety, a fluorescence-quenching

- 3 moiety, a radioactive moiety, a radiopaque moiety, a paramagnetic moiety, a nanoparticle, a
- 4 vesicle, a molecular beacon, a marker, a marker enzyme, a contrast agent, a chemotherapeutic
- 5 agent, and a radiation-sensitizer.
- 1 15 (original): The molecule of claim 14, wherein the cargo portion C comprises 2 a contrast agent for diagnostic imaging.
- 1 16 (original): The molecule of claim 14, wherein the cargo portion C comprises 2 a radiation sensitizer for radiation therapy.
- 1 (original): The molecule of claim 11, wherein said peptide portion A
 2 comprises about 5 to about 9 glutamates or aspartates.
- 1 18 (original): The molecule of claim 17, wherein said peptide portion A
 2 comprises about 5 to about 9 consecutive glutamates or aspartates.
- 1 19 (original): The molecule of claim 11, wherein said portion peptide **B** 2 comprises between about 9 to about 16 arginines.
- 20 (original): The molecule of claim 19, wherein said peptide portion **B**comprises between about 9 to about 16 consecutive arginines.
- 1 21 (original): The molecule of claim 11, wherein said peptide portion A
 2 comprises D-amino acids.
- 1 22 (original): The molecule of claim 11, wherein said peptide portion **B** comprises D-amino acids.
- 1 23 (original): The molecule of claim 11, wherein said peptide portion A consists of D-amino acids.
- 1 24 (original): The molecule of claim 11, wherein said peptide portion **B** consists of D-amino acids.

1	25 (original): The molecule of claim 11, wherein said peptide portions A and B
2	consist of D-amino acids.
1	26 (original): The molecule of claim 25, wherein said peptide portion B consists
2	of D-arginine amino acids.
1	27 (original): The molecule of claim 11, wherein said peptide portion A is
2	located at a terminus of a polypeptide chain comprising $\mathbf{B} - \mathbf{C}$.
1	28 (original): The molecule of claim 11, wherein said peptide portion A is
2	located at the amino terminus of a polypeptide chain comprising $\mathbf{B} - \mathbf{C}$.
1	29 (original): The molecule of claim 11, wherein said peptide portion A is linked
2	near to or at the amino terminus of a polypeptide chain comprising $\mathbf{B} - \mathbf{C}$.
1	30 (original): The molecule of claim 11, wherein said peptide portion A is linked
2	near to or at the carboxy terminus of a polypeptide chain comprising $\mathbf{B} - \mathbf{C}$.
1	31 (original): The molecule of claim 11, wherein $\mathbf{B} - \mathbf{C}$ comprises a polypeptide
2	chain having ends consisting of a B-side terminus and a C-side terminus, and wherein cleavable
3	linker X is disposed near or at said B-side terminus.
1	32 (original): The molecule of claim 11, wherein $\mathbf{B} - \mathbf{C}$ comprises a polypeptide
2	chain having ends consisting of a B-side terminus and a C-side terminus, and wherein cleavable
3	linker X is disposed near or at said C-side terminus.
	33-36 (canceled)
1	37 (original): The molecule of claim 11, wherein cleavable linker X comprises
2	aminocaproic acid.
	38-44 (canceled)

1	45 (original): The molecule of claim 11, comprising a plurality of cleavable
2	linkers X linking a portion A to a structure $B - C$.
1	46 (currently amended): A pharmaceutical composition comprising:
2	A molecule of the structure $A - X - B$, wherein
3	B is a peptide portion of about 5 to about 20 basic amino acid residues, which is
4	suitable for cellular uptake,
5	A is a peptide portion of about 2 to about 20 acidic amino acid residues, which
6	when linked with portion $\bf B$ is effective to inhibit or prevent cellular uptake of portion $\bf B$, and
7	X is a cleavable linker of about 3 to about 30 atoms joining A with B , which can
8	be cleaved under physiological conditions, wherein X comprises the sequence of SEQ ID NO: 1;
9	and
10	a pharmaceutically acceptable carrier.
1	47 (previously presented): The pharmaceutical composition of claim 46, wherein
2	said portion A has between about 5 to about 9 acidic amino acid residues, and said
3	portion B has between about 9 to about 16 basic amino acid residues.
1	48 (original): The pharmaceutical composition of claim 46 or 47, further
2	comprising a portion C covalently attached to said portion B and comprising a cargo moiety.
1	49 (withdrawn): A method of modulating cellular uptake of a peptide B of about
2	5 to about 20 basic amino acid residues, which is suitable for cellular uptake, comprising:
3	linking said peptide B to a peptide A of about 2 to about 20 acidic amino acid
4	residues with a cleavable linker X of about 3 to about 30 atoms, which can be cleaved under
5	physiological conditions and
6	cleaving said cleavable linker X effective to separate peptide B from molecule A .
1	50 (withdrawn): A method of modulating cellular uptake of a cargo moiety C,
2	comprising:

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3	covalently attaching a cargo moiety C to a peptide B of about 5 to about 20 basic
4	amino acid residues to form a molecule $\mathbf{B} - \mathbf{C}$;
5	linking said molecule $\mathbf{B} - \mathbf{C}$ to a peptide \mathbf{A} of about 2 to about 20 acidic amino
6	acid residues with a cleavable linker X of about 3 to about 30 atoms, and
7	cleaving said cleavable linker X effective to separate $B - C$ from said peptide A .
1	51 (withdrawn): A nucleic acid encoding a molecule of the structure $A - X - B$,
2	wherein
3	B is a peptide of about 5 to about 20 basic amino acid residues, which is suitable
4	for cellular uptake,
5	A is a peptide of about 2 to about 20 acidic amino acid residues, which when
6	linked with peptide $\bf B$ is effective to inhibit or prevent cellular uptake of peptide $\bf B$, and
7	X is a cleavable linker portion of between 1 and 10 amino acid residues joining A
8	with B, which can be cleaved under physiological conditions.
1	52 (withdrawn): A nucleic acid encoding a molecule of the structure $\mathbf{A} - \mathbf{X} - \mathbf{B}$
1 2	52 (withdrawn): A nucleic acid encoding a molecule of the structure $\mathbf{A} - \mathbf{X} - \mathbf{B} - \mathbf{C}$, wherein
2	C, wherein
2	C, wherein C is a peptide cargo moiety,
2 3 4	 C, wherein C is a peptide cargo moiety, B is a peptide of about 5 to about 20 basic amino acid residues, which is suitable
2 3 4 5	 C, wherein C is a peptide cargo moiety, B is a peptide of about 5 to about 20 basic amino acid residues, which is suitable for cellular uptake,
2 3 4 5 6	 C, wherein C is a peptide cargo moiety, B is a peptide of about 5 to about 20 basic amino acid residues, which is suitable for cellular uptake, A is a peptide of about 2 to about 20 acidic amino acid residues, which when
2 3 4 5 6 7	 C, wherein C is a peptide cargo moiety, B is a peptide of about 5 to about 20 basic amino acid residues, which is suitable for cellular uptake, A is a peptide of about 2 to about 20 acidic amino acid residues, which when linked with peptide B is effective to inhibit or prevent cellular uptake of peptide B - C, and
2 3 4 5 6 7 8	 C, wherein C is a peptide cargo moiety, B is a peptide of about 5 to about 20 basic amino acid residues, which is suitable for cellular uptake, A is a peptide of about 2 to about 20 acidic amino acid residues, which when linked with peptide B is effective to inhibit or prevent cellular uptake of peptide B - C, and X is a cleavable linker portion of between 1 and 10 amino acid residues joining A
2 3 4 5 6 7 8	C, wherein C is a peptide cargo moiety, B is a peptide of about 5 to about 20 basic amino acid residues, which is suitable for cellular uptake, A is a peptide of about 2 to about 20 acidic amino acid residues, which when linked with peptide B is effective to inhibit or prevent cellular uptake of peptide B - C, and X is a cleavable linker portion of between 1 and 10 amino acid residues joining A with B - C which can be cleaved under physiological conditions.

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4	B is a peptide portion of about 5 to about 20 basic amino acid residues, which is
5	suitable for cellular uptake, is covalently linked to portion C, and is effective to enhance
6	transport of cargo portion C across a cell membrane,
7	${f Q}$ is a quencher moiety attached to ${f A}$ and effective to quench fluorescence from
8	fluorescent cargo C;
9	A is a peptide portion of about 2 to about 20 acidic amino acid residues, which
10	when linked with portion B is effective to inhibit or prevent cellular uptake of $\mathbf{B} - \mathbf{C}$, and
11	X is a cleavable linker of about 2 to about 100 atoms joining A with $\mathbf{B} - \mathbf{C}$, which
12	can be cleaved under physiological conditions.

54 -55 (canceled)

56 (original): The molecule of claim 11, comprising a single cargo portion **C**linked to a plurality of portions **B**, each of portions **B** being linked to a cleavable linker portion **X**linked to an acidic portion **A**.